REMARKS/ARGUMENTS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

At the outset, Applicants acknowledge with appreciation the Examiner's indications that the restriction requirement has been withdrawn, and that claim 39 is allowable in substance. Applicants believe that with the amendments above, the remaining claims are also allowable.

Claims 29, 32, 33, 35, and 53 have been amended to replace the language "a small and/or polar amino acid residue" by a list of suitable amino acids, that list being "an amino acid residue selected from the group consisting of serine, alanine, glycine, valine, threonine, aspartic acid, glutamic acid, arginine, lysine, histidine, asparagine, glutamine and tyrosine." The third paragraph on page 22 of the specification lists serine, alanine, glycine, valine and threonine as *preferred* small and/or polar amino acid residues. In addition, the second paragraph on the same page identifies aspartic acid, glutamic acid, arginine, lysine, asparagine and glutamine as examples of polar amino acids. Further, histidine and tyrosine were the other polar amino acids well known to the artisan at the time of the present invention, as evidenced by Alberts et al., in the online version of *Molecular Biology of the Cell,* Garland Science (2002), a copy of which is attached to the accompanying information disclosure statement.

Claim 29 has also been amended to add two closely related sequences amino acids 20 to 144 of SEQ ID NO: 2; and 1 to 129 of SEQ ID NO: 8. These changes are supported by the

specification on page 22, second paragraph, and in the paragraph bridging pages 12-13.

In view of the amendment to claim 29, claim 30 has been canceled and claim 31 made dependent on claim 29.

Claim 32 has also been made independent, except that Applicants are now claiming that the soluble protein consists in part of either amino acid residues 20 to 144 of SEQ ID NO:2 (rather than 20 to 145, previously); or amino acid residues 1 to 129 of SEQ ID NO:8 (rather than 1 to 130, previously), and one or more amino acid residues derived from the neighboring intracellular domain at the C-terminus. These changes are supported by, for example, the paragraph bridging pages 12-13 of the specification; the paragraph bridging pages 21-22 of the specification, and by SEQ ID NOs:2 and 8.

Claim 37 has been made dependent on claim 36, and specifies that substitution is at the *third* cysteine. This amendment is supported by the specification at page 8, paragraph "(3)"; page 9, paragraph "(10)"; page 22, second full paragraph; in conjunction with the location of the cysteines in the CD83 extracellular region as shown for example in Figure 1 and in the sequence listing, *e.g.*, SEQ ID NO:2.

Claim 49 has been amended to provide a list of specific indications, which are supported by, for example, the specification in point 6 at the bottom of page 8, and in the paragraph bridging pages 13-14.

Claim 53 has been amended to claim that the soluble protein consists of amino acid

residues 1 to 130 of SEQ ID NO:8, wherein the third cysteine, i.e., residue 85, is substituted with serine. This change is supported as for claim 37.

Finally, new claims 54 and 55 are added. Claim 54 is supported as above for claim 37. Claim 55 is supported by Figure 8, showing the sequence, and Example 9, pages 46-47, discussing results obtained with "hCD83ext_mut 129_Cys to Ser," which is a substitution of the fifth cysteine.

Applicants do not believe that any of the amendments introduce new matter. An early notice to that effect is earnestly solicited.

The application was objected to as failing to comply with the applicable Sequence Listing rules in failing to include the sequence "Gly-Ser-Pro-Gly." In response, Applicants submit a substitute page 10 of the paper Sequence Listing, including the sequence "Gly-Ser-Pro-Gly," and a substitute Computer Readable Form (CRF). The undersigned hereby certifies that the substitute sheet of the paper Sequence Listing does not introduce new matter, and that the content of the substitute CRF is identical to the substitute paper Sequence Listing. Applicants have also amended the specification at page 11, Figure 8 legend; page 13, first paragraph; and page 22, first paragraph, to include the sequence identifier for the sequence "Gly-Ser-Pro-Gly."

The original declaration was objected to as being defective due to non-initialed and/or non-dated alterations. In response, Applicants respectfully request that this issue be held in abeyance. Applicants have forwarded a substitute declaration to the inventors for execution, and

the substitute declaration will be filed as soon as received back from abroad. See, 37 CFR § 1.111(b) ("[A] request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated.")

Claim 32 was objected to under 37 CFR § 1.75(c) as failing to limit the subject matter of a further claim from which it depends. In response, as noted above, Applicants have rewritten claim 32 in independent form.

Claims 29, 32, 33, 35-38, 46, 49-51 and 53 were rejected under 35 USC § 112, second paragraph, as being indefinite. In response, as noted above, Applicants have replaced the phrase "small and/or polar amino acids" by a list of specific amino acids supported mainly by the specification and, additionally, in the case of histidine and tyrosine, by knowledge well known in the art at the time of the invention.

Claim 53 was rejected under 35 USC § 112, first paragraph, as claiming new matter. In response, as noted above, Applicants have amended claim 53 in a manner that moots the Examiner's concern.

Claims 29-33, 35-37, 46, 49-51 and 53 were rejected under 35 USC §112, first paragraph, as being broader than the enabling disclosure. The Examiner appears to have two concerns. First, the Examiner finds that the specification does not enable the use of variants other than where the fifth cysteine residue is substituted. Second, the Examiner finds that the specification

does not enable any method of use other than a method of treating multiple sclerosis.

In response, Applicants respectfully submit the accompanying Declaration of Dr. Charles Nicolette, who is the Chief Scientific Officer and Vice President, Research and Development, of the assignee of the present application, Argos Therapeutics, Inc.

In numbered paragraph 3, Dr. Nicolette reports the successful experimental results of a variant wherein the *third* cysteine residue is substituted in a kidney transplant rejection model. Dr. Nicolette concludes that "[e]xamination of the transplanted kidneys in each group showed that the transplants in the CD83 group retained normal histology at the end of the experiment, while tissue from the untreated control group showed histology indicating severe rejection."

In numbered paragraph 4, Dr. Nicolette reports the successful results of the *same variant* in a model for irritable bowel disease induced in the model by administration of dinitrobenzenesulfonic acid (DNBS). Dr. Nicolette reports that "[h]istological examination showed that the evident damage resulting from DNBS administration was prevented by sCD83."

In numbered paragraph 5, Dr. Nicolette reports the successful results of experimental results of the variant wherein the *fifth* cysteine residue is substituted in a model of insulin-dependent diabetes mellitus. Dr. Nicolette concludes that "[f]ive of six CD83-treated mice did not develop diabetes during the course of the experiment, while 5 of 8 of the untreated NOD mice did develop diabetes, demonstrating that CD83 can block the onset of diabetes in this model."

Collectively, these data establish that (1) substitution at other than the fifth cysteine is also operable; and (2) the variants can be used to treat a variety of diseases or medical conditions in addition to multiple sclerosis. These data confirm and support the statements made in the specification, and provide reasonable assurance that the entire scope originally claimed will operate as indicated in the original specification. Nevertheless, in order to advance the prosecution, and without prejudice, Applicants have limited method claim 49 to a small list of indications clearly supported by the data now of record, Morbus Crohn (Crohn's disease) and colitis ulcerosas (ulcerative colitis) being examples of irritable bowel diseases. Of course, any successful single experimental result supports the enablement for the product claims.

In view of the foregoing, Applicants respectfully submit that the Examiner's enablement concerns have been proven to be unjustified. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection, and allow the present claim scope.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,

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